

MR 5-DOSE VIALS

TOTAL SYSTEMS EFFECTIVENESS ANALYSIS

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GLOSSARY

Category	Indicator	Description
Analysis	Total systems effectiveness	A holistic approach used to prioritize or decide between products from a systems perspective, taking into consideration coverage, equity, programmatic implications, and full systems cost.
	Comparative analysis	The analysis that directly compares the outputs of targeting 1 million children with 5-dose vials versus 10-dose vials.
	Gavi 73 market analysis	The analysis that provides a broader Gavi 73 market perspective of the impact of countries switching to 5-dose vials across various uptake scenarios (described in Table 2).
Vaccine Delivery	Total required supply	The demand for M and MR considering target population, number of doses, coverage, and wastage rate.
	Number of children vaccinated	The number of M and MR doses administered to children, including both MCV1 and MCV2 doses.
	Number of doses wasted	The number of doses wasted out of the total required supply, based on the wastage rates.
Total Systems Costs	Vaccine price	The vaccine price per dose, as reported by UNICEF.
	Vaccine procurement price per vaccinated child	The vaccine price per dose administered, adjusted for wastage.
	Incremental non-vaccine costs per vaccinated child	The additional annual costs per dose administered associated with switching from 10-dose to 5-dose vials. Additional costs take into account cold chain, transport, outreach, human resources, and wastage disposal costs. Data came from the DPCP Zambia report.
	Total costs per vaccinated child	The wastage-adjusted vaccine procurement price per vaccinated child. For 5-dose vials, this also includes the incremental non-vaccine costs per vaccinated child.
	Weighted average price	The average price of measles-containing vaccine (MCV) weighted by the share of M and MR 5- and 10-dose vials.
	Weighted average price per vaccinated child	The weighted average price, adjusted for wastage.
Cold Chain Requirements	Cold chain per dose	Cold chain volume required per dose (in cm ³) from the Gavi detailed product profiles.
	Cold chain per vaccinated child	Cold chain volume per dose administered, adjusted for wastage.

OVERVIEW

Total Systems Effectiveness (TSE) is a holistic approach used to prioritize or decide between products from a systems perspective, taking into consideration **coverage, equity, programmatic implications, and full systems cost.**

A data-driven TSE analysis was conducted to articulate the public health value of measles (M) and measles-rubella (MR) 5-dose (5d) vials. While 5-dose vials have been proposed as a way to lower wastage and increase coverage compared to 10-dose (10d) vials, they are also associated with higher costs and greater cold chain requirements. This analysis attempts to quantify the programmatic, financial, and logistical trade-offs between 5-dose and 10-dose vials.

The TSE analysis used available data to incorporate assumptions on the impact of 5-dose vials on factors such as coverage, wastage, price, programmatic costs, cold chain requirements, and other qualitative considerations. The analysis is not intended for country decision-making; rather, it is meant to inform stakeholder conversations on the development of an action plan for measles 5-dose vials.

ANALYSES, SCENARIOS, CONCEPTUAL MODEL

The TSE analyses include two different models: a comparative analysis and a Gavi 73 market analysis

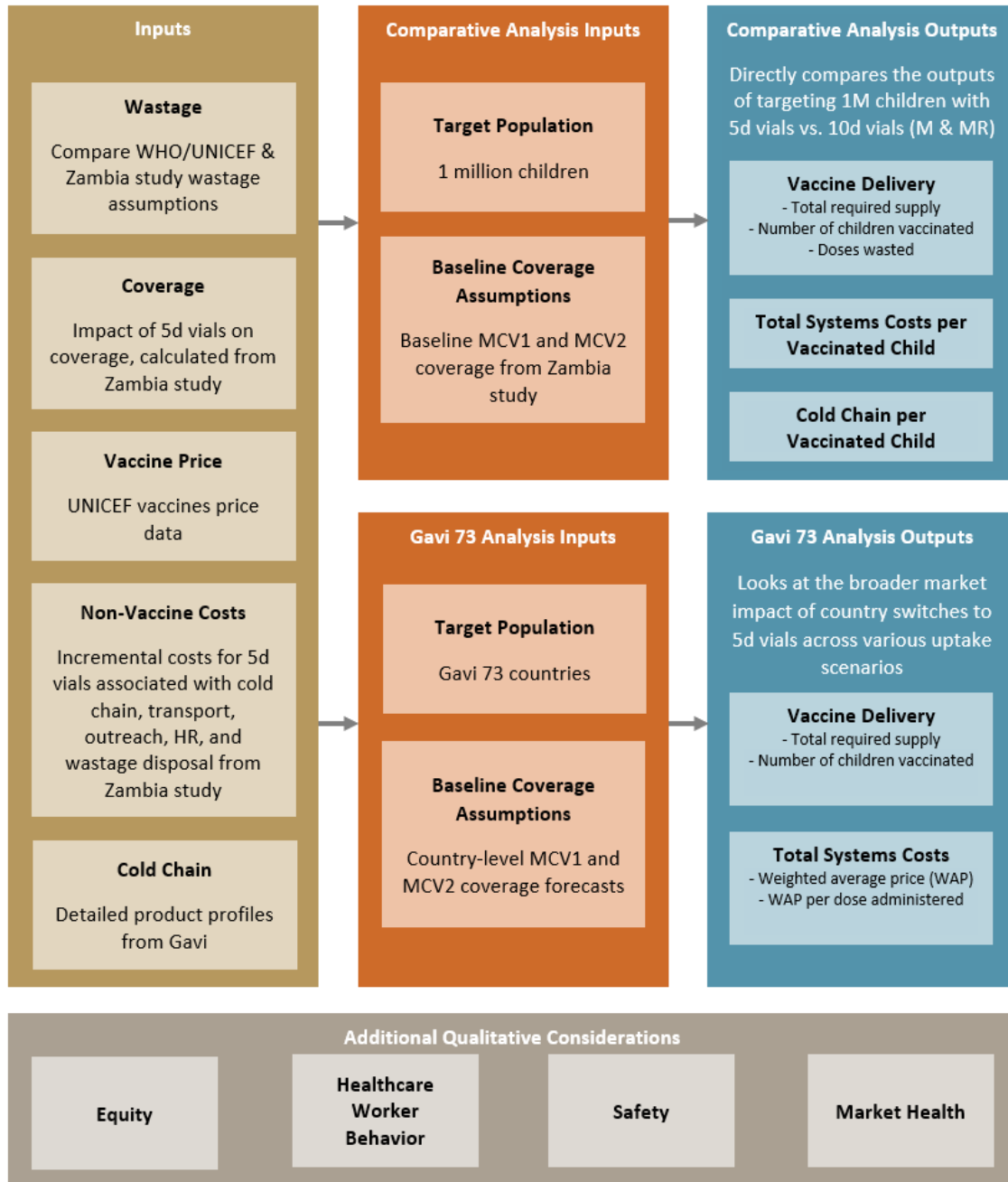
Table 1: Overview of the two analysis models

Model	Asumptions
<p>Comparative Analysis</p> <p><i>This analysis directly compares the outputs of targeting 1 million children with 5-dose vials versus 10-dose vials</i></p>	<ul style="list-style-type: none"> The outputs of this analysis are dependent on wastage and baseline coverage assumptions This analysis was run using two different wastage assumptions for 5d and 10d vials (WHO/UNICEF Fact Sheet wastage assumptions and Zambia study wastage results) We assume the same baseline coverage rates that were found in the intervention arm of the Zambia study (MCV1 = 82.1%, MCV2 = 43.0%) We also conducted a sensitivity analysis to explore the trade-offs between the reduction in wastage and the incremental increase in non-vaccine costs per dose associated with 5d vials
<p>Gavi 73 Market Analysis</p> <p><i>This analysis provides a broader Gavi 73 market perspective of the impact of countries switching to 5-dose vials across various uptake scenarios (described in Table 2)</i></p>	<ul style="list-style-type: none"> This analysis forecasts demand for 2021 – 2030 To calculate demand and inform uptake assumptions, the model incorporates data from the Global Vaccine Market Model, the Zambia study on the switch to MR 5-dose vials, and expert intel This analysis only looked at routine immunization (RI) demand and not campaign demand, since 5d vials are expected to have a greater impact in RI settings

Table 2: Gavi 73 Market Analysis uptake scenarios

Base Uptake	Medium Uptake	High Uptake
<p>Only countries that have introduced 5d already or are expected to switch to 5d vials, based on expert intel:</p> <ul style="list-style-type: none"> Comoros Eritrea India Laos Lesotho Myanmar São Tomé Timor-Leste 	<p>Base uptake scenario, plus countries with the greatest number of unimmunized MCV children (adjusted as needed based on expert intel):</p> <ul style="list-style-type: none"> Afghanistan Angola Bangladesh Chad DRC Ethiopia Indonesia Madagascar Nigeria 	<ul style="list-style-type: none"> All Gavi countries using M or MR gradually switch to 5d vials between 2021 and 2030

CONCEPTUAL MODEL



KEY FINDINGS

Vaccine Characteristics	Outcomes	Impact				Key Takeaways
		EI	CF	GC	LT MH	
Coverage 	Number of children vaccinated 	●	●	●	●	<ul style="list-style-type: none"> Healthcare workers are more likely to open 5-dose vials, leading to increased coverage and more children vaccinated Increased routine immunization (RI) coverage may lead to reduced need for costly campaigns and improved demand predictability
Wastage 	Total required supply 	●	●	●	●	<ul style="list-style-type: none"> Since 5-dose vials reduce wastage, countries can vaccinate more children with less total required supply (TRS)
Vaccine price per dose 	Vaccine price per vaccinated child 	●	●	●	●	<ul style="list-style-type: none"> Although the UNICEF price per dose is higher for 5-dose vials, after adjusting for wastage, the vaccine procurement price per vaccinated child is only slightly higher for 5-dose vials
Incremental non-vaccine costs per vaccinated child 	Total costs per vaccinated child 	●	●	●	●	<ul style="list-style-type: none"> 5-dose vials are associated with incremental non-vaccine costs such as cold chain, transport, outreach, human resources (HR), and wastage disposal compared to 10-dose vials Incremental costs were mostly associated with HR costs in the Zambia study
Cold chain (cm³) per dose 	Net cold chain per vaccinated child (cm³) 	●	●	●	●	<ul style="list-style-type: none"> Despite the higher cold chain per dose for 5-dose vials, the reduced TRS helps to offset the cold chain requirements The Zambia study found that the difference in net cold chain per immunized child is marginal and 5-dose vials had minimal impact on the cold chain

▼ = 10-dose vials ▼ = 5-dose vials

Large negative impact
 Small negative impact
 Marginal impact
 Small positive impact
 Large positive impact

EI – Equity impact **GC** – Gavi costs
CF – Country feasibility **LTMH** – Long-term market health

INPUTS AND ASSUMPTIONS

WASTAGE RATES

Given the uncertainty of the impact of 5-dose vials on wastage, and the various factors that influence wastage, this analysis compared two different sources for wastage assumptions:

- The WHO/UNICEF Measles and Measles-Rubella (MR) Vaccine Five-Dose Vial Presentations Fact Sheet 2021
- The results from the Zambia study (Krudwig et al., 2020)
 - Please refer to the Zambia study for additional information on the wastage results

Table 3: Wastage rate assumptions

Source	10d vial wastage	5d vial wastage	Difference
WHO/UNICEF Fact Sheet	40%	30%	10%
Zambia Study	30.53%	16.18%	14.35%

COVERAGE RATES

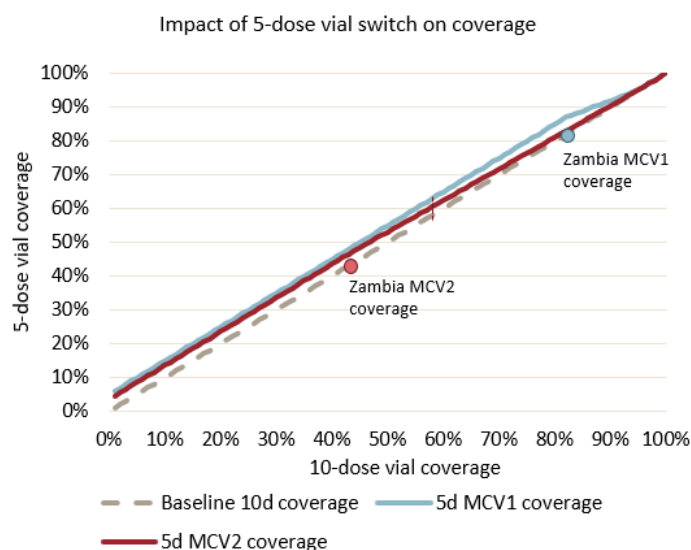
- There is little data available on the impact of switching to 5-dose vials on coverage
- The Zambia study found that the 5-dose vial intervention increased MCV1 coverage by 4.9% and MCV2 coverage by 3.5%
- For the baseline coverage assumptions in the comparative analysis, we used the MCV1 and MCV2 coverage of the intervention arm from both the vaccination card and the caregiver's recall
 - Please refer to Table 5 in the *Vaccine Zambia study* for additional information

Table 4: Impact of 5d vials on coverage from Zambia

Vaccine	Baseline coverage	Intervention effect
MCV1	82.1%	+ 4.9%
MCV2	43.0%	+ 3.5%

- We modeled the intervention effect across different baseline MCV1 and MCV2 coverage rates
- We applied the intervention effect (+ 4.9% for MCV1, + 3.5% for MCV2) to baseline coverage up to 82.1% for MCV1 and 43.0% for MCV2
- Beyond the baseline coverage found in the Zambia study, we assumed diminishing returns, with eventually no intervention effect once baseline coverage reaches 95%
- As baseline MCV coverage increases, the impact of switching to 5-dose vials on coverage decreases
- Figure 1 shows 10-dose vial MCV coverage and the corresponding 5-dose vial MCV1 and MCV2 coverage

Figure 1: Estimating the impact of 5-dose vials on MCV1 and MCV2 coverage



COSTS

Vaccine price

- Vaccine price per dose information is from the [UNICEF Vaccines pricing data](#)
- Prices are shown in Table 5
- Note that for measles 10-dose vials, we used SII's price per dose (\$0.35) rather than Bio Farma's (\$0.25), so we considered the maximum price per dose
- The vaccine price per dose was adjusted for wastage to calculate the vaccine procurement price per vaccinated child

Incremental non-vaccine costs

- The incremental non-vaccine costs per dose administered associated with switching from 10-dose to 5-dose vials was taken from the Dose Per Container Partnership (DPCP) Zambia report
- The Zambia study took into consideration the following factors:
 - Cold chain costs
 - Transport costs for vaccine collection
 - Outreach costs (excluding human resource costs)
 - Human resource costs
 - Wastage disposal
- The incremental annual costs for storage, transport, human resources, outreach, and wastage disposal associated with switching to 5-dose vials were \$0.11 per dose of vaccine administered
 - Most health facilities reported no change in incremental costs, so the interquartile range (IQR) of costs is \$0.00 – \$0.05
 - The upper interquartile (\$0.05) can be considered to account for possible overestimation of human resource costs due to study requirements
- Please refer to the DPCP Zambia report for additional information on non-vaccine costs
- The incremental non-vaccine costs per dose administered were added to the 5-dose vial vaccine procurement price per vaccinated child to calculate the total costs per vaccinated child (including vaccine price and all incremental non-vaccine costs)

Table 5: Vaccine and non-vaccine cost assumptions

Cost assumptions	Measles			Measles-Rubella		
	10d vial	5d vial (IQR)	Diff.	10d vial	5d vial (IQR)	Diff.
UNICEF price per dose	\$0.35	\$0.43	\$0.08	\$0.72	\$0.90	\$0.18
Incremental non-vaccine costs per dose administered	\$0.00	\$0.11 (\$0.00 – \$0.05)	\$0.11	\$0.00	\$0.11 (\$0.00 – \$0.05)	\$0.11

COLD CHAIN

- Cold chain per dose assumptions come from the Gavi detailed product profiles resource
- Cold chain per vaccinated child was calculated to adjust for wastage and coverage

Table 6: Cold chain assumptions

Cold Chain (cm ³)	Measles				Measles-Rubella				
	10d vial		5d vial	Diff.	10d vial		5d vial		Diff.
Manufacturer	SII	Bio Farma	SII		SII	BioE	SII	BioE	
Cold chain per dose	5.25	5.83	9.70	3.87 – 4.45	5.24	3.90	9.71	5.92	0.68 – 5.81

RESULTS

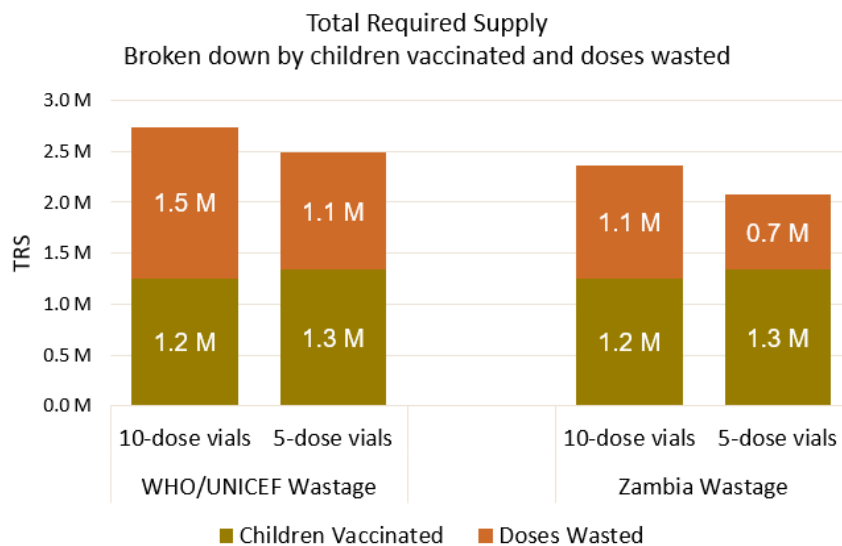
VACCINE DELIVERY

Comparative analysis

Targeting 1 million children with 5-dose vials results in lower total required supply (TRS), more children vaccinated, and fewer doses wasted than with 10-dose vials.

- These results are seen using both the WHO/UNICEF wastage assumptions and the Zambia study wastage assumptions
- As a reminder, the results below assume baseline coverage rates that were found in the intervention arm in the Zambia study (MCV1 = 82.1%, MCV2 = 43.0%). The exact ratio of children vaccinated to doses wasted varies depending on baseline coverage; however, the same pattern shown in Figure 2 is seen across baseline coverage assumptions.

Figure 2: TRS broken down by children vaccinated and doses wasted



Market analysis

As more Gavi 73 countries adopt 5-dose vials, countries can vaccinate more children through routine immunization while decreasing the total required supply.

- Figure 3 shows that as more countries adopt 5-dose vials, the TRS decreases compared to the base scenario
 - TRS is affected by wastage assumptions, so the results for both the WHO/UNICEF and Zambia wastage assumptions are shown
- Figure 4 shows that as more countries switch to 5-dose vials, the number of children vaccinated increases
- Comparing the outputs of the Zambia wastage assumptions to the base scenario in 2030:
 - The medium scenario requires 8.2 million fewer doses and vaccinates 1.8 million additional children
 - The high scenario requires 18.6 million fewer doses and vaccinates 3.2 million additional children

Figure 3: Gavi 73 TRS across different 5-dose uptake and wastage assumptions

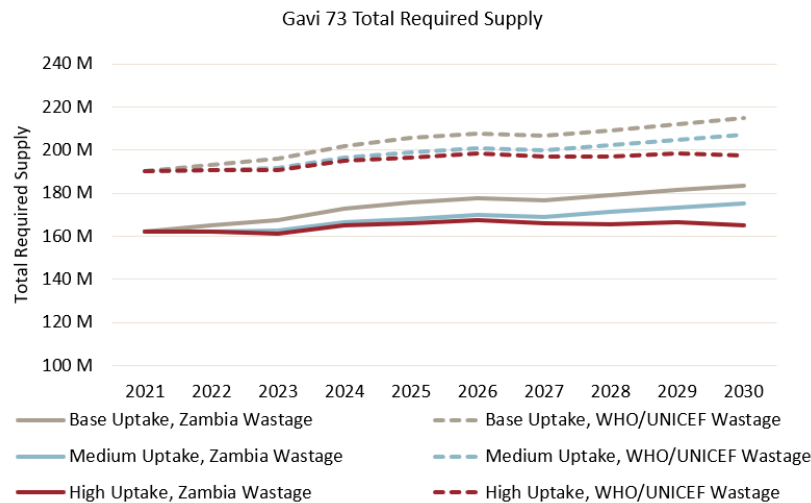
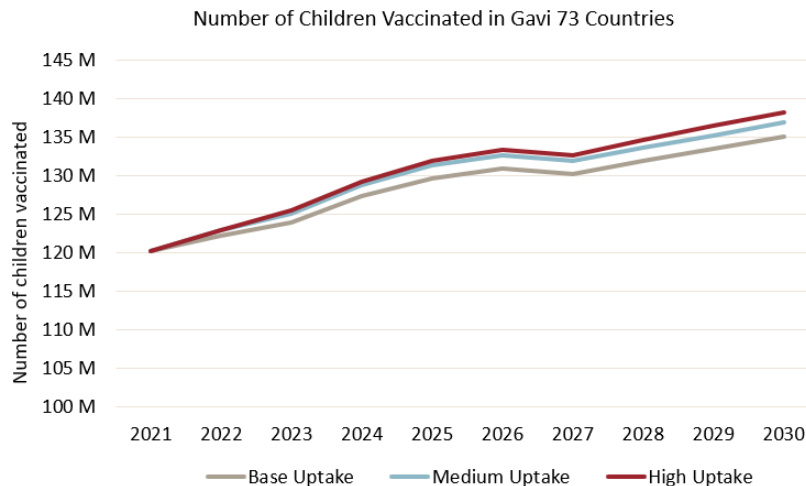


Figure 4: Number of children vaccinated in Gavi 73 countries across different 5-dose uptake scenarios



TOTAL SYSTEMS COSTS

Comparative analysis

After adjusting for wastage, the vaccine procurement price per vaccinated child is marginally higher for 5-dose vials.

- This result is seen using both the WHO/UNICEF and Zambia study wastage assumptions (Figures 5 & 6)
- The range in difference between 10-dose vials and 5-dose vials of M and MR using the different wastage assumptions is \$0.01 – \$0.10

The 5-dose vials have higher total costs per vaccinated child—mostly attributable to incremental non-vaccine costs.

- The total costs per vaccinated child include the vaccine price and all incremental non-vaccine costs associated with switching to 5-dose vials
- The Zambia study found that switching to 5-dose vials is associated with an incremental increase in costs for storage, transport, human resources, outreach, and wastage
 - There was no change in cold chain costs attributable to switching to 5-dose vials
 - There were relatively minimal costs associated with transport, outreach, and sharps waste disposal
 - Human resources time had the largest impact on incremental costs and was attributed to time conducting fixed immunization sessions, conducting stock management, and reporting

Improving RI coverage could reduce the need for campaigns and associated costs.

- It was out of the scope of this analysis to quantify, but theoretically, the increased RI measles coverage could reduce the need for costly campaigns and improve demand predictability.

Figure 5: Total costs per vaccinated child – measles

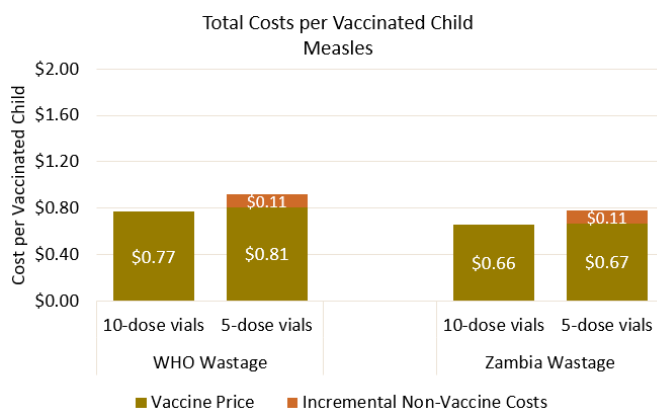
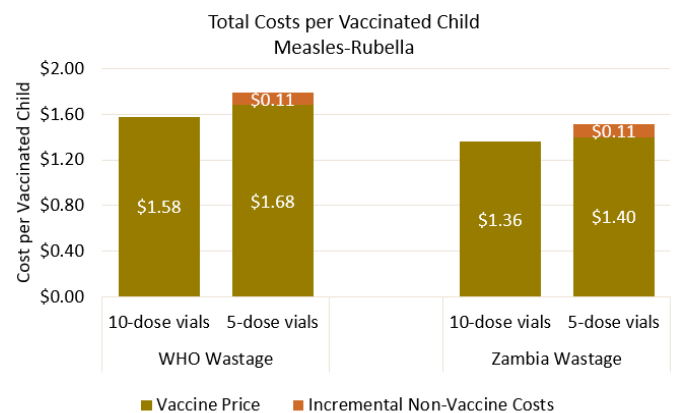


Figure 6: Total costs per vaccinated child – measles-rubella



Sensitivity analysis

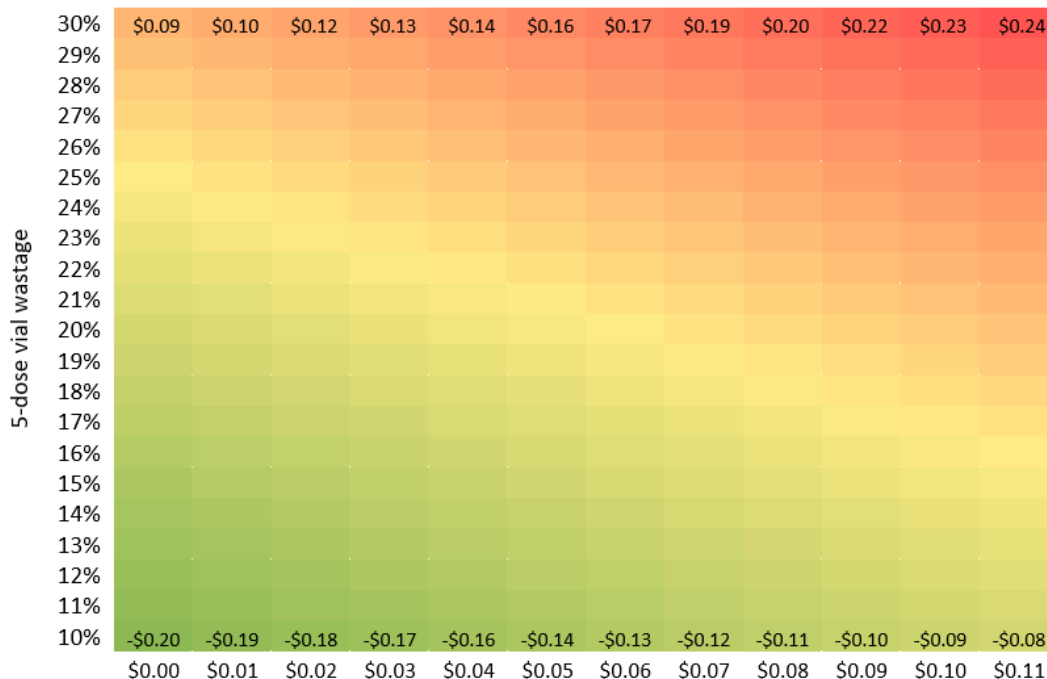
Given the uncertainty of the impact of 5-dose vials on wastage and incremental non-vaccine costs, we conducted a sensitivity analysis to explore when the total costs per vaccinated child for MR 5-dose vials break even with MR 10-dose vials.

- Using the WHO/UNICEF wastage assumptions, we assumed 10-dose vial wastage of 40% and looked at a range of outcomes for 5-dose vial wastage between 10% and 30%
- For incremental non-vaccine costs, we looked at a range of \$0.00 to \$0.11 to account for the average incremental costs from the Zambia study for 5-dose vials (\$0.11) and the interquartile range (\$0.00 – \$0.05)
- Figure 7 shows a heat map of the difference in total systems costs per dose administered between MR 5-dose and 10-dose vials across different wastage and incremental cost assumptions
 - When the cells are red (as in the upper right), the total systems costs for 5-dose vials are greater than the costs for 10-dose vials
 - When the cells are green (as in the lower left), the total systems costs for 5-dose vials are less than the costs for 10-dose vials
 - When the cells are yellow (in the middle), the total systems cost per dose administered break even

As incremental non-vaccine costs for 5-dose vials increase, a larger decrease in wastage is needed to break even with 10-dose vial costs.

- Assuming 40% 10-dose vial wastage, and the average incremental non-vaccine costs per dose from the Zambia study (\$0.11), 5-dose vial wastage would need to drop to 16% to be equivalent in costs to 10-dose vials

Figure 7: Estimated costs or savings per dose administered attributable to switching to 5-dose vials across different wastage and incremental non-vaccine cost assumptions



Market analysis

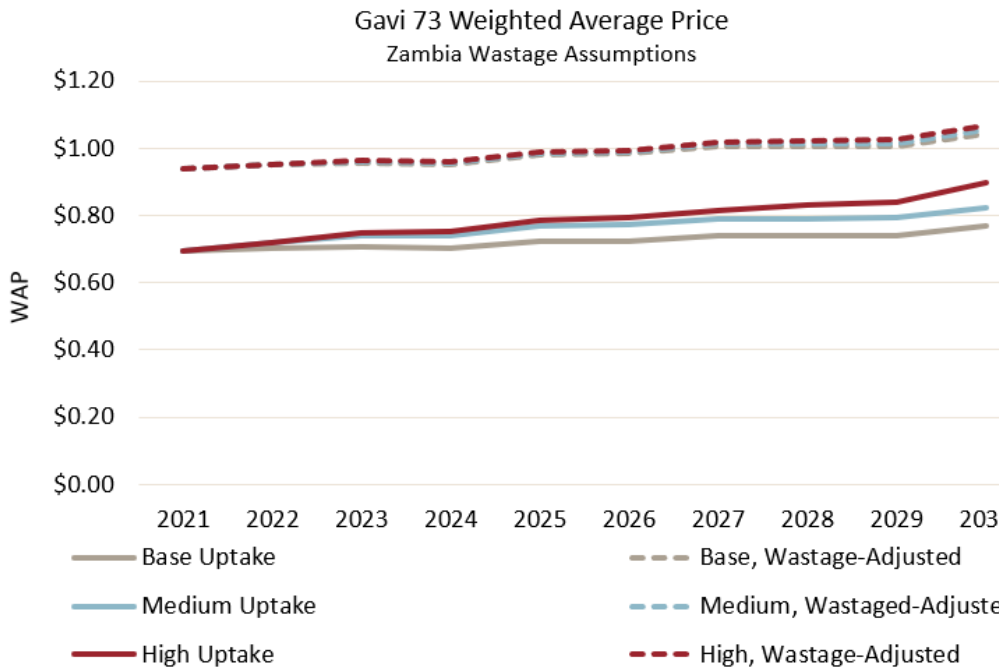
As more countries adopt 5-dose vials, the weighted average price (WAP) increases, since 5-dose vials cost more per dose.

- The range in WAP in 2030 is \$0.77 (base uptake) to \$0.90 (high uptake)

After adjusting for wastage and coverage, the WAP per vaccinated child is essentially equivalent across the uptake scenarios.

- The range in WAP per dose administered in 2030 is \$1.04 (base uptake) to \$1.07 (high uptake)
- The wastage-adjusted results were comparable using the WHO/UNICEF and Zambia study wastage results, so Figure 8 only shows the results using the Zambia study wastage assumptions.

Figure 8: Gavi 73 WAP and WAP per vaccinated child



COLD CHAIN REQUIREMENTS

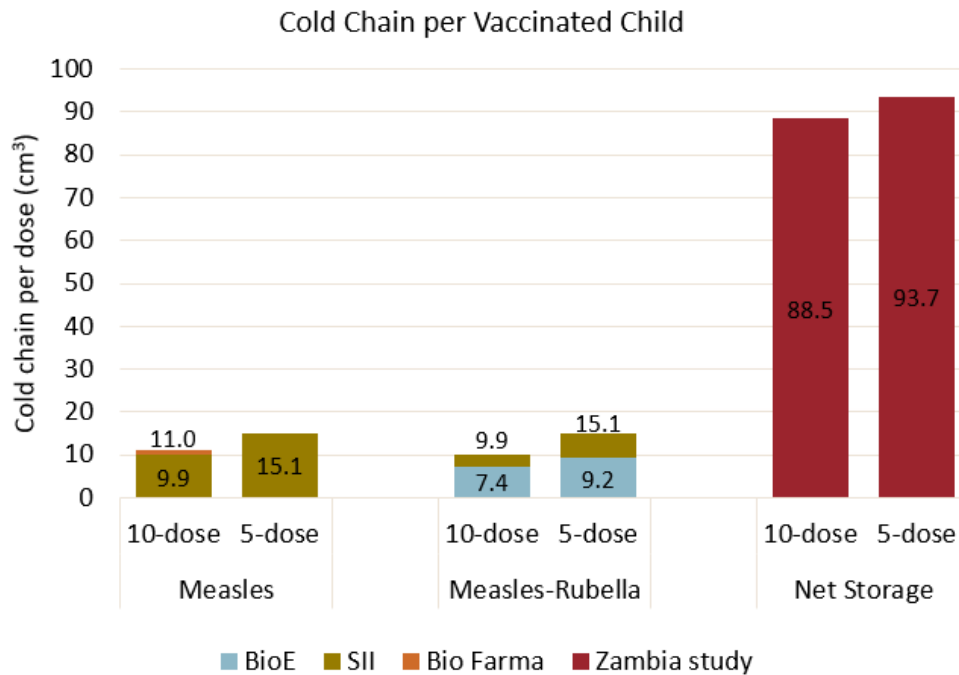
While 5-dose vials take up more cold chain space per dose, this is offset by the lower total required supply, and all health facilities in the Zambia study had sufficient cold chain space.

- M and MR 5-dose vials take up more space per dose than 10 dose-vials
- The lower wastage rates and total required supply of 5-dose vials helps to offset the discrepancy in cold chain requirements, because healthcare facilities need to store fewer doses
 - Figure 9 shows the wastage-adjusted cold chain per dose administered using the Zambia wastage assumptions

The Zambia study found that the difference in total net storage requirement per fully immunized child, including the vaccine, was marginal.

- The Zambia study looked at the net storage required per fully immunized child, considering cold boxes, vaccine carriers, and refrigerators
- All health facilities in the intervention arm had sufficient cold chain space for the increase in volume required for introducing 5-dose MR vials

Figure 9: Cold chain requirements per vaccinated child



ADDITIONAL CONSIDERATIONS

Equity

- MR 5-dose is a delivery-based innovation that can help reach un-/under-immunized children, especially in rural and remote areas where session sizes tend to be small
- Minimizing missed opportunities for vaccination will help drive progress towards achieving equity goals in immunization

Healthcare worker behavior

- Despite open vial policies that promote ‘one vial one child,’ healthcare worker reluctance to open vials remains a challenge in routine immunization
- MR 5-dose will reduce healthcare worker hesitancy to open a vial due to fear of wastage and/or stockouts
- Use of 5-dose will improve timely coverage and reduce missed opportunities for vaccination, while also limiting wastage

Safety

- Increasing the doses per container increases the opportunity for user error, which may raise the likelihood of non-sterile injections and injections with expired vaccine. MR 5-dose could help reduce this risk.
- Respondents from the Zambia study and stakeholders from our interviews expressed concerns about mixing vial sizes and diluents when there are multiple presentations at a given health facility. However, most stakeholders believe effective training and communications will minimize this risk and none of the respondents at health facilities in the Zambia study mentioned reports from communities about adverse events following immunization.

Market health

- Interviewees mentioned that supply sustainability for MR 5-dose should not be a challenge given the capacity of manufacturers in the market. It will be important to provide adequate market signaling to manufacturers so that there is sufficient and reliable supply for countries that introduce 5-dose.
- If demand for MR 5-dose is sufficiently high, then the price per dose could decrease and become more cost-effective for countries
- MR 5-dose is an intervention that would improve routine immunization coverage, thus hopefully reducing countries’ reliance on campaigns and minimizing the unpredictability of supply year-over-year

LIMITATIONS

Wastage

- Limited data is available on the impact of MR 5-dose vials on wastage rates
- Many factors can influence wastage, and the context of each country should be taken into consideration

Coverage

- Limited data is available to understand the impact of 5-dose vials on coverage in different settings, such as health facilities with varying catchment population sizes

Total costs

- There is uncertainty around the incremental programmatic costs associated with switching to 5-dose vials, and costs will vary in different contexts

Cold chain

- The impact of switching to 5-dose vials on the cold chain is uncertain and will vary for each health facility

Zambia study

- The Zambia study was used to inform assumptions on wastage, coverage, incremental cost, and cold chain
- Please reference the Zambia study for a complete description of study limitations

RESOURCES

- [WHO/UNICEF: Measles and Measles-Rubella \(MR\) Vaccine Five-Dose Vial Presentations Fact Sheet 2021](#)
- [Vaccine Article: The effects of switching from 10 to 5-dose vials of MR vaccine on vaccination coverage and wastage: A mixed method study in Zambia.](#)
- [Dose Per Container Partnership: Implementing 5-dose Measles-Rubella Vaccine Vials in Zambia—Research Findings](#)
- [Gavi Detailed Product Profiles \(DPPs\) for WHO prequalified Vaccines](#)
- [UNICEF MR vaccine prices](#)
- [UNICEF M vaccine prices](#)